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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,005	03/26/2004	Dana P. Gaddy	022438.45889	7761

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/810,005	GADDY, DANA P.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 21* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20071008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

The Information Disclosure Statement (IDS) filed 8 October 2007 is acknowledged. Applicant's amendment of the claims filed 15 August 2007 has been entered.

Claims 20 and 22 have been cancelled. Claims 1-19 and 21 are pending. Claims 1-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Claims 19 and 21 are under examination.

Claim Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The amended claims 19 and 21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath et al. (U.S. Patent No: 5,674,844), in view of Cassidy

et al. (U.S. Patent No: 6,280,474 B1) for reasons of record in the previous office action and below.

The amended claims are now drawn to a method for increasing cancellous bone strength and bone volume in a human subject comprising administering in a soluble form of an effective amount of human inhibin A or human inhibin B in a pharmaceutically acceptable carrier to the human subject (claims 19 and 21).

Applicant argues that the '844 patent discloses a treatment to prevent loss of and increase bone mass in metabolic diseases by administering a morphogen which includes a long list of potential morphogens, and inhibin/activin are among those. Applicant argues that the data in the '844 patent provide support for a dimeric protein comprising a sequence having at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1 (residues 38-139 of SEQ ID NO: 5) or a sequence having a generic sequence 6 (SEQ ID NO: 31), however, sequence alignment between the human OP-1 fragment with inhibin α subunit and activin β A subunit which, when combined with the inhibin α subunit, comprises Inhibin A, does not satisfy the 70% homology required by the '844 patent. Applicant argues that inhibin A and B do not fall within the definition of the proteins that the '844 patent taught had beneficial properties. Applicant further argues that in the laundry list of morphogens, activin is disclosed in conjunction with inhibin, however, Applicant has disclosed that activin did not work for the claimed use, and the signaling pathway initiated by the use of inhibins is different from that of activin or BMPs. Applicant argues that because activin operates in the opposite manner according to applicant's experiments, there is no level of predictability

with respect to the claimed invention. Applicant also argues that the '474 patent discloses an implant for tissue repair made of a dehydrated crosslinked biocompatible polymer, and that the '474 patent does not disclose the use of soluble recombinant inhibin A without a polymer carrier to increase bone formation.

Applicant's arguments have been fully considered but have not been found to be persuasive.

As set forth in the previous office actions, the '844 patent specifically discloses that inhibin proteins formulated with a pharmaceutically acceptable carrier can be used to increase bone mass or prevent bone loss in a human patient afflicted with a bone disease, such as osteoporosis resulting from malignant transformations. Although the "844 patent discloses OP-1 polypeptides as a preferred embodiment to increase bone formation, inhibin proteins can also been used for the same therapeutic purpose. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998). Patents are relevant as prior art for all they contain. The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)).

With regard to the argument that activins do not work for the claimed use and operate in the opposite manner according to applicant's experiments and that the signaling pathways initiated by inhibins and activins are different, numerous evidence indicates that activin stimulates bone formation. For example, Gaddy-Kurten et al. (Endocrinol., 2002, 143(1): 74-83) reviewed some of these studies and stated that activin has been shown to be osteogenic in several *in vivo* systems, similar to the BMPs; Local administration of activin increases periosteal bone matrix thickness in newborn rat parietal bone and enhances noncartilagenous ectopic bone formation stimulated by BMP2; and in addition, activin (0.4–10 μg/d) promotes fracture healing when administered locally to rat fibula (see pp. 81, section "Activin actions on bone *in vitro* and *in vivo*"). As for the mode of action, Hirotani et al. (Calcif. Tissue Int., 2002, 70:330-338) reported that activin A is involved in both bone formation and bone resorption, however, it is possible that activin A may primarily affect bone formation rather than bone resorption because mice with grafted bone exhibited an increase in bone mass upon activin A treatment. Although the mechanism mediated by inhibins is different from that of activin or BMPs, however, these proteins can be used in the same therapeutic applications, i.e., to stimulate bone formation and increase bone strength, which as been disclosed in the '844 patent and demonstrated to be enabled by the art.

With regard to the amendment that the inhibins are in a soluble form, the '844 patent teaches that morphogens may be prepared in different forms, for example, a soluble form suitable for parenteral injections (column 20, line 64 through column 21, line 30).

Based on the reasons set forth above and previously, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the '844 patent, with those of the '474 patent to use inhibin A or inhibin B for increasing bone mass or preventing bone loss in a human afflicted with a bone disease. One of ordinary skill in the art would have been motivated to combine the teachings, because the '844 patent teaches that inhibin proteins can be used to increase bone mass or preventing bone loss, and the '474 patent teaches that inhibin A and inhibin B can be used in an implant to facilitate bone repair and promote new bone formation. Therefore, the teachings provide a reasonable expectation of successfully increasing bone strength and bone volume in a patient.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER

Xiaozhen Xie, Ph. D.
October 31, 2007